PENDING CLAIMS

5. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain adjacent to said detection position and a second target domain comprising said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP); and

ii) a first target-specific sequence comprising a first base at an interrogation position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed wherein at least one of said first and second ligation probes comprises an adapter sequence;

c) removing non-hybridized probes;

d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

f) contacting said amplicons with an array of capture probes; and

g) determining the nucleotide at said detection position.

9. (Amended) A method according to claim 5 , 26, 32 and 33 wherein said removing comprises:

a) enzymatically adding a binding ligand to said target sequence to form a target sequence comprising said binding ligand;

b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;

c) washing away unhybridized probes; and

d) eluting said probes off said solid support.

10. A method according to claim 5, 26, 32, or 33 wherein said removing is done using a double-stranded specific moiety.

11. A method according to claim 10 wherein said double-stranded specific moiety is an intercalator attached to a support.

12. A method according to claim 11 wherein said support is a bead.

13. A method according to claim 5, 26, 32, or 33 wherein said amplifying is done by:

a) hybridizing a first universal primer to said UUP;

b) providing a polymerase and dNTPs such that said first universal primer is extended;

c) hybridizing a second universal primer to said DUP;

d) providing a polymerase and dNTPs such that said second universal primer is extended; and

e) repeating steps a) through d).

14. A method according to claim 5, 26, 32, or 33 wherein said array comprises:

a) a substrate with a patterned surface comprising discrete sites; and

b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.

15. A method according to claim 14 wherein said discrete sites comprise wells.

16. A method according to claim 14 wherein said substrate comprises a fiber optic bundle.

19. (Amended) A method according to claim 5 or 32, further comprising providing a support on which the target sequence is immobilized.

20. (Amended) A method according to claim 19, wherein said non-hybridized probes are removed without removing said target sequence from said support.

21. (Amended) A method according to claim 5 or 32, further comprising attaching said target sequence to a support.

22. (Amended) A method according to claim 21, wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety that binds said support, absorption of said target sequence on a charged support, direct chemical attachment of said target sequence to said support and photocrosslinking said target sequence to said support.

23. (Amended) A method according to claim 9, wherein said support is selected from the group consisting of paper, plastic and tubes.

26. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain adjacent to said detection position and a second target domain comprising said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;

b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP); and

ii) a first target-specific sequence comprising a first base at an interrogation position; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;

d) removing non-hybridized probes;

e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

f) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

g) contacting said amplicons with an array of capture probes; and

h) determining the nucleotide at said detection position.

30. (New) A method according to claim 9 wherein said solid support is a bead.

31. (New) A method according to claim 26 wherein said non-hybridized probes are removed without removing said target sequence from said support.

32. (New) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP);

ii) a first target-specific sequence; and

iii) an interrogation position that is complementary to said detection position; and

b) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, wherein at least one of said first and second ligation probes comprises an adapter sequence;

c) removing non-hybridized probes;

d) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

e) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

f) contacting said amplicons with an array of capture probes; and

g) determining the nucleotide at said detection position.

33. (New) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;

b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP);

ii) a first target-specific sequence; and

iii) an interrogation position; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and

ii) a second target-specific sequence;

whereby if said interrogation position of said first probe is perfectly complementary to said nucleotide at said detection position, a ligation complex is formed, and wherein at least one of said first and second ligation probes comprises an adapter sequence;

d) removing non-hybridized probes;

e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

f) amplifying said ligated probe using said UUP and said DUP to generate a plurality of amplicons;

g) contacting said amplicons with an array of capture probes; and

h) determining the nucleotide at said detection position.

34. (New) A method according to claim 15, wherein said substrate comprises a fiber optic bundle.